American Osteopathic Association
Continuing Medical Education

CERTIFICATION OF HOME STUDY

This is to certify that I, _____ completed the following activity for AOA CME credits.
Please print

Type of activity (such as reading or listening) _____

Name of journal(s) *or* audio-tape and date(s) of issue(s): _____

_____

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(One-half CREDIT may be granted for each issue or tape)

_____ _____
AOA number D.O.'s signature

_____ _____
College and year of graduation Current address (including zip code)

MAIL TO: AOA Division of CME, 212 East Ohio Street, Chicago, Illinois 60611

KEEP A DUPLICATE FOR YOUR RECORDS!

The **Home Study** form is intended to document individual reading of recognized scientific journals, listening to approved audio-tapes, and other approved home study courses and programs under the criteria described for Category **2-B.**

Only one type of home study, such as reading, should be indicated on a single form, though multiple issues of scientific journals may be listed.

This form should **not** be used, however, when CME quiz cards for the AOA Journal are submitted separately.

FOR OFFICE USE ONLY
Cat. 2-B Credits _____
Date _____
Program # _____
Doctor # _____
Doctor's Name _____

Please refer to the revised CME GUIDE for additional information.

Form Revised: 1/77

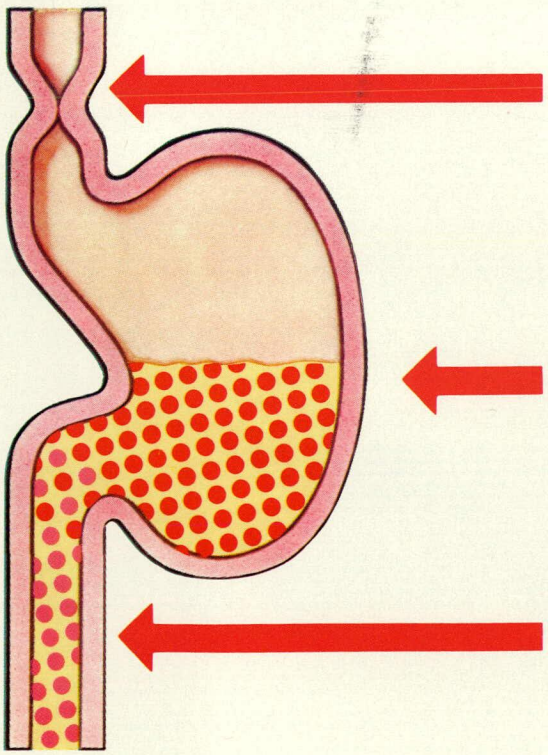
A unique therapeutic approach to the common problem of:

REFLUX
REFLUX
REFLUX

REGLAN®

(Metoclopramide Hydrochloride)

Tablets 10 mg; Syrup 5 mg/5mL



Increases lower esophageal sphincter pressure to prevent gastroesophageal reflux

Improves gastric emptying of food and acid to reduce contents available for reflux

Coordinates antroduodenal contractions to **prevent bile reflux**

A·H·ROBINS

Pharmaceutical Division, Richmond, Virginia 23261-6609

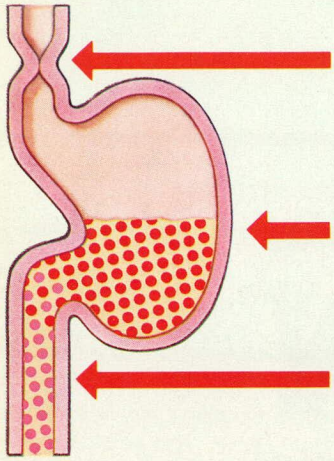
Please see following page for prescribing information.

For Effective Reflux Relief

When results are unsatisfactory with conventional measures alone

SPECIFY **REGLAN**® Tablets 10 mg Syrup 5 mg/5 mL

(Metoclopramide HCl)



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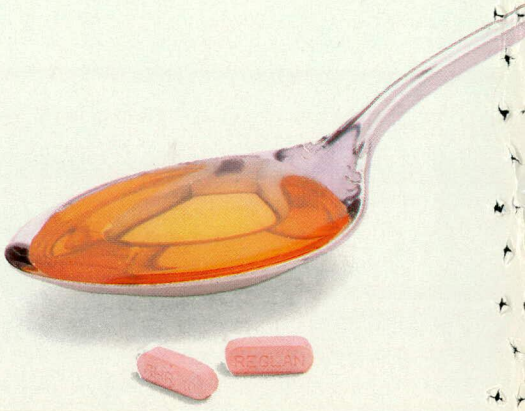

Side Effects: The most common side effects are restlessness, drowsiness, fatigue and lassitude, which occur in approximately 10 percent of patients receiving the most commonly prescribed dosage of 10 mg q.i.d. At this dosage, extrapyramidal symptoms occur in approximately 1 in 500 patients.

Tablets 10 mg

Available in bottles of 100 (NDC 0031-6701-63) and 500 tablets (NDC 0031-6701-70) and Dis-Co® Unit Dose Packs of 100 tablets (NDC 0031-6701-64).

Syrup 5 mg/5 mL

Available in pints (NDC 0031-6706-25) and 10 mL Dis-Co® Unit Dose Packs (10 x 10s) (NDC 0031-6706-26).

The following is a brief summary only. Before prescribing, see complete prescribing information in Reglan product labeling.

Indications and Usage: ***Symptomatic gastroesophageal reflux:*** Reglan Tablets are indicated as short-term (4 to 12 weeks) therapy for adults with symptomatic, documented gastroesophageal reflux who fail to respond to conventional therapy.

The principal effect of metoclopramide is on symptoms of postprandial and daytime heartburn with less observed effect on nocturnal symptoms. If symptoms are confined to particular situations, such as following the evening meal, use of metoclopramide as single doses prior to the provocative situation should be considered, rather than using the drug throughout the day. Healing of esophageal ulcers and erosions has been endoscopically demonstrated at the end of a 12-week trial using doses of 15 mg q.i.d. As there is no documented correlation between symptoms and healing of esophageal lesions, patients with documented lesions should be monitored endoscopically.

Contraindications: Metoclopramide should not be used whenever stimulation of gastrointestinal motility might be dangerous, e.g., in the presence of gastrointestinal hemorrhage, mechanical obstruction, or perforation.

Metoclopramide is contraindicated in patients with pheochromocytoma because the drug may cause a hypertensive crisis, probably due to release of catecholamines from the tumor. Such hypertensive crises may be controlled by phentolamine.

Metoclopramide is contraindicated in patients with known sensitivity or intolerance to the drug.

Metoclopramide should not be used in epileptics or patients receiving other drugs which are likely to cause extrapyramidal reactions, since the frequency and severity of seizures or extrapyramidal reactions may be increased.

Warnings: Depression bearing a temporal relationship to Reglan administration has been reported.

Extrapyramidal symptoms, manifested primarily as acute dystonic reactions, occur in approximately 1 in 500 patients treated with the usual adult dosages of 30–40 mg/day of metoclopramide. These usually are seen during the first 24–48 hours of treatment with metoclopramide, occur more frequently in children and young adults, and are even more frequent at the higher doses used in prophylaxis of vomiting due to cancer chemotherapy. These symptoms may include involuntary movements of limbs and facial grimacing, torticollis, oculogyric crisis, rhythmic protrusion of tongue, bulbar type of speech, trismus, or dystonic reactions resembling tetanus. Rarely, dystonic reactions may present as stridor and dyspnea, possibly due to laryngospasm. If these symptoms should occur, inject 50 mg Benadryl® (diphenhydramine hydrochloride) intramuscularly, and they usually will subside. Cogentin® (benztropine mesylate), 1 to 2 mg intramuscularly, may also be used to reverse these reactions.

Parkinsonian-like symptoms have occurred, more commonly within the first 6 months after beginning treatment with metoclopramide, but occasionally after longer periods. These symptoms generally subside within 2–3 months following discontinuance of metoclopramide.

Tardive Dyskinesia: Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with metoclopramide. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to predict which patients are likely to develop the syndrome. Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase with the duration of treatment and the total cumulative dose.

Less commonly, the syndrome can develop after relatively brief treatment periods at low doses; in these cases, symptoms appear more likely to be reversible.

There is no known treatment for established cases of tardive dyskinesia although the syndrome may remit, partially or completely, within several weeks-to-months after metoclopramide is withdrawn. Metoclopramide itself, however, may suppress (or partially suppress) the signs of tardive dyskinesia, thereby masking the underlying disease process. The effect of this symptomatic suppression upon the long-term course of the syndrome is unknown. Therefore, the use of metoclopramide for the symptomatic control of tardive dyskinesia is not recommended.

Precautions: ***General.*** Metoclopramide may impair the mental and/or physical abilities required for the performance of hazardous tasks such as operating machinery or driving a motor vehicle. The ambulatory patient should be cautioned accordingly.

In one study in hypertensive patients, intravenously administered metoclopramide was shown to release catecholamines; hence, caution should be exercised when metoclopramide is used in patients with hypertension.

Drug Interactions. The effects of metoclopramide on gastrointestinal motility are antagonized by anticholinergic drugs and narcotic analgesics. Additive sedative effects can occur when metoclopramide is given with alcohol, sedatives, hypnotics, narcotics or tranquilizers.

The finding that metoclopramide releases catecholamines in patients with essential hypertension suggests that it should be used cautiously, if at all, in patients receiving monoamine oxidase inhibitors.

Absorption of drugs from the stomach may be diminished (e.g., digoxin) by metoclopramide, whereas absorption of drugs from the small bowel may be accelerated (e.g., acetaminophen, tetracycline, levodopa, ethanol).

Gastroparesis (gastric stasis) may be responsible for poor diabetic control in some patients. Exogenously administered insulin may begin to act before food has left the stomach and lead to hypoglycemia. Because the action of metoclopramide will influence the delivery of food to the intestines and thus the rate of absorption, insulin dosage or timing of dosage may require adjustment.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 77-week study was conducted in rats in oral doses up to about 40 times the maximum recommended human daily dose. Metoclopramide elevates prolactin levels and the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin-dependent *in vitro*, a factor of potential importance if the prescription of metoclopramide is contemplated in a patient with previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating drugs, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms has been found in rodents after chronic administration of prolactin-stimulating neuroleptic drugs and metoclopramide. Neither clinical studies nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is too limited to be conclusive at this time.

An Ames mutagenicity test performed on metoclopramide was negative.

Pregnancy Category B. Reproduction studies performed in rats, mice, and rabbits by the i.v., i.m., s.c. and oral routes at maximum levels ranging from 12 to 250 times the human dose have demonstrated no impairment of fertility or significant harm to the fetus due to metoclopramide. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers. Metoclopramide is excreted in human milk. Caution should be exercised when metoclopramide is administered to a nursing mother.

Adverse Reactions: In general, the incidence of adverse reactions correlates with the dose and duration of metoclopramide administration. The following reactions have been reported, although in most instances, data do not permit an estimate of frequency:

CNS Effects. Restlessness, drowsiness, fatigue and lassitude occur in approximately 10% of patients receiving the most commonly prescribed dosage of 10 mg q.i.d. (see Precautions). Insomnia, headache, confusion, dizziness or depression (see Warnings) occur less frequently. In cancer chemotherapy patients being treated with 1–2 mg/kg per dose, incidence of drowsiness is about 70%. There are isolated reports of convulsive seizures without clearcut relationship to metoclopramide. Rarely, hallucinations have been reported.

Extrapyramidal Reactions (EPS). Acute dystonic reactions, the most common type of EPS associated with metoclopramide, occur in approximately 0.2% of patients (1 in 500) treated with 30 to 40 mg of metoclopramide per day. In cancer chemotherapy patients receiving 1–2 mg/kg per dose, the incidence is 2% in patients over the ages of 30–35, and 25% or higher in children and young adults who have not had prophylactic administration of diphenhydramine. Symptoms include involuntary movements of limbs, facial grimacing, torticollis, oculogyric crisis, rhythmic protrusion of tongue, bulbar type of speech, trismus, opisthotonus (tetanus-like reactions) and rarely, stridor and dyspnea possibly due to laryngospasm; ordinarily these symptoms are readily reversed by diphenhydramine (see Warnings).

Parkinsonian-like symptoms may include bradykinesia, tremor, cogwheel rigidity, mask-like facies (see Warnings).

Tardive dyskinesia most frequently is characterized by involuntary movements of the tongue, face, mouth or jaw, and sometimes by involuntary movements of the trunk and/or extremities (see Warnings).

Motor restlessness (akathisia) may consist of feelings of anxiety, agitation, jitteriness, and insomnia, as well as inability to sit still, pacing, foot-tapping. These symptoms may disappear spontaneously or respond to a reduction in dosage.

Endocrine Disturbances. Galactorrhea, amenorrhea, gynecomastia, impotence secondary to hyperprolactinemia (see Precautions). Fluid retention secondary to transient elevation of aldosterone (see Clinical Pharmacology).

Cardiovascular. Hypotension, hypertension and a single instance of supraventricular tachycardia (see Contraindications, Precautions).

Gastrointestinal. Nausea and bowel disturbances, primarily diarrhea.

Renal. Urinary frequency and incontinence.

Hematologic. A few cases of neutropenia, leukopenia, or agranulocytosis, generally without clearcut relationship to metoclopramide.

Allergic Reactions. A few cases of rash, urticaria, or bronchospasm, especially in patients with a history of asthma. Rarely, angioneurotic edema, including glossal or laryngeal edema.

Miscellaneous. Visual disturbances. Porphyria. Rare occurrences of neuroleptic malignant syndrome (NMS) have been reported. This potentially fatal syndrome is comprised of the symptom complex of hyperthermia, altered consciousness, muscular rigidity and autonomic dysfunction.

Transient flushing of the face and upper body, without alterations in vital signs, following high doses intravenously.

Overdosage: Symptoms of overdosage may include drowsiness, disorientation and extrapyramidal reactions. Anticholinergic or antiparkinson drugs or antihistamines with anticholinergic properties may be helpful in controlling the extrapyramidal reactions. Symptoms are self-limiting and usually disappear within 24 hours.

Hemodialysis removes relatively little metoclopramide, probably because of the small amount of the drug in blood relative to tissues. Similarly, continuous ambulatory peritoneal dialysis does not remove significant amounts of drug. It is unlikely that dosage would need to be adjusted to compensate for losses through dialysis. Dialysis is not likely to be an effective method of drug removal in overdose situations.

Literature reports describe methemoglobinemia in premature and full term neonates who were given metoclopramide intramuscularly, 1–2 mg/kg/day for 3 or more days. Methemoglobinemia has not been reported in similar infants treated with 0.5 mg/kg/day in divided doses. Methemoglobinemia can be reversed by the intravenous administration of methylene blue.

Dosage and Administration: ***For the relief of symptomatic gastroesophageal reflux:*** Administer from 10 mg (1 tablet) to 15 mg (1½ tablets) up to q.i.d. 30 minutes before each meal and at bedtime, depending upon symptoms being treated and clinical response (see Clinical Pharmacology and Indications). If symptoms occur only intermittently or at specific times of the day, use of metoclopramide in single doses up to 20 mg prior to the provoking situation may be preferred rather than continuous treatment.

Experience with esophageal erosions and ulcerations is limited, but healing has thus far been documented in one controlled trial using q.i.d. therapy at 15 mg/dose, and this regimen should be used when lesions are present, so long as it is tolerated (see Adverse Reactions). Because of the poor correlation between symptoms and endoscopic appearance of the esophagus, therapy directed at esophageal lesions is best guided by endoscopic evaluation.

Therapy longer than 12 weeks has not been evaluated and cannot be recommended.

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